Inflammatory Pseudotumors of the Skull Base

Abstract—Inflammatory pseudotumor is a rare affliction of the skull base with a propensity for locally aggressive growth. Frequently, the location of involvement does not lend itself to conventional biopsy techniques, resulting in diagnostic and treatment dilemma. A retrospective review of three unusual cases of skull base inflammatory pseudotumors is reported. These lesions illustrate the difficulty of management by virtue of their histopathology and behavior. They are clinically and radiographically indistinguishable from invasive neoplasms. One involved the petrous apex with bony erosion; a second case presented with pain and trigeminal paresthesia secondary to an infiltrative lesion in the clivus and the sphenoid sinus; and the third case involved peritubal soft tissues of the infratemporal fossa, with mandibular paresthesia and middle ear effusion. All three lesions were resected via lateral skull base approaches with no evidence of recurrence. Because of the inherent nature of this lesion and its rarity, inflammatory pseudotumor should remain a diagnosis of exclusion. When suspected, surgical approaches should be designed to allow complete extirpation with limited morbidity. (*Skull Base Surgery*, 4(2):93–98, 1994)

Inflammatory pseudotumor is an idiopathic condition characterized by the onset of sclerosing inflammation which clinically and radiographically mimicks a neoplastic process. It is by and large an affliction of the orbit with very infrequent extensions into contiguous extraorbital structures.^{1–6} Although primary involvement of other organ systems has been recognized,^{7–10} pseudotumors received little attention in the otolaryngologic literature until recent years. Pseudotumors have been found in the larynx, maxillary sinus, parapharyngeal space, temporal bone, and the infratemporal fossa^{11–14}; however, treatment has been varied and inconsistent.

Pseudotumors occurring in the skull base either as an extension of orbital disease or as a primary lesion have the propensity to behave very aggressively, frequently with bony erosion and cranial neuropathy.^{1,2,4,5,11,12,14} Both clinical and radiographic manifestations may be compatible with that of a malignant process. This clinical ambiguity is compounded by the relative inaccessibility of the skull base in obtaining biopsy specimens.

The purpose of this article is to report three cases of inflammatory pseudotumor affecting the skull base. These

cases illustrate the locally invasive nature of a condition that is highly suggestive of a malignancy. In view of this aggressiveness, it is important to obtain tissues that are truly representative of the lesion for histologic assessment. Surgical approaches should be designed to provide a safe and oncologically sound access for diagnostic biopsy, with the option to carry out a complete resection.

CASE REPORTS

Case 1 (CR)

A 15-year-old boy presented in April 1989 with a 3-year history of intermittent right sided otorrhea and otalgia. A series of failed medical treatments led to an unspecified middle ear and mastoid operation in 1988 without success. Two months prior to referral he experienced episodes of dizziness and imbalance upon manipulation of the right tragus. He was noted to have a positive fistula sign in the right ear by the referring physician. Physical examination on admission revealed polypoid tis-

sues and secretion filling the middle ear. A fistula sign was not present and the patient had no vestibular symptoms. His left ear was normal, and the rest of the exam revealed no abnormalities. He had no evidence of cranial neuropathy. An audiogram demonstrated a cochlear reserve of about 30 dB and a superimposed maximal conductive hearing loss in the right ear. His hearing was normal in the left ear.

Computed tomography (CT) and magnetic resonance imaging (MRI) displayed a well demarcated, infiltrative lesion involving the right petrous apex and peritubal space (Figs. 1A, B). There was a cystic component to the tumor with rim enhancement on CT scan, displacing the middle fossa dura superiorly. It appeared bright on both T1 and T2 weighted MRI, and partially encased the petrous carotid artery. However, it was relatively avascular on angiography, abutting against the vertical portion of the petrous carotid artery without eroding the carotid canal.

Cultures of the ear discharge produced mixed organisms including *Streptococcus pneumoniae* and *Pseudomonas*; acid fast staining for tuberculosis was negative.

An abnormally high level of serum alkaline phosphatase of 563 U/L (normal: 30–150 U/L) was attributed to bony erosion. A biopsy of the aural polyp showed subacute inflammation with a dominant eosinophilia that was non-diagnostic. Because of the atypical presentation, the possibility of a malignancy, especially rhabdomyosarcoma, was considered. A subtotal petrosectomy¹⁵ was performed with preservation of the otic capsule and the facial nerve.

Polypoid tissues partially filled the middle ear and extended into the supralabyrinthine and infralabyrinthine regions; a cystic cavity was encountered in the petrous apex. A frozen section was suggestive but not diagnostic of rhabdomyosarcoma. Given this uncertainty, a radical resection was not carried out, but all abnormal-appearing tissues were removed by widely exenterating all pneumatic spaces. The surgical cavity was obliterated, and the external meatus permanently closed.

A pronounced lymphoplasmocellular inflammation, eosinophilia, sparse necrosis, and a telangiectatic fibrous reaction were found in all the specimens submitted. No histiocytes were identified on S-100 protein immuno-

Figure 1. A: Axial computed tomography scan of the temporal bone showing an erosive and expansile mass (arrows) within the petrous apex. B: Coronal magnetic resonance image (T1 weighted) demonstrating the tumor (T) with extension into the middle fossa (arrows). C: Lymphoplasmocellular infiltration with significant fibrosis on hematoxylin and eosin stain.

stain, and anti-desmin and anti-myoglobin antibodies were negative for rhabdomyosarcoma. There were no granulomas and no evidence of bacterial, fungal, or parasitic infection. The final diagnosis was that of a chronic lymphoplasmocellular inflammation of the temporal bone, compatible with an inflammatory pseudotumor (Fig. 1C). No further treatment was instituted, and the patient has been well for 2½ years without recurrence.

Case 2 (MD)

A 10-year-old boy presented in December 1989 with a 6-month history of intermittent left sided watery rhinorrhea, which had become blood stained for 6 weeks. He had also experienced general malaise and left sided headaches. On examination, there were trigeminal paresthesia involv-

ing the maxillary and mandibular divisions, left ptosis, and no other regional or systemic abnormalities. An infiltrative lesion was demonstrated on CT involving the clivus and the sphenoid sinus. There were extensions along the left lateral skull base involving the peritubal space, the foramen ovale, and the horizontal portion of the petrous carotid artery. MRI confirmed the extent of this lesion, demonstrating bright signals on T1 weighted images with gadolinium enhancement (Fig. 2A) and mixed signals on T2. A transnasal sphenoid biopsy demonstrated chronic inflammatory changes; this was not thought to be representative of the lesion. Given this rapidly progressive and invasive process, treatment could not be instituted without a definitive histologic diagnosis. The proximity of the lesion to the petrous carotid artery was considered a limiting factor and would render any surgical attempt hazardous if not properly secured. A balloon occlusion was

Figure 2. A: Coronal magnetic resonance image (T1 weighted) with gadolinium enhancement. An infiltrative lesion (T) involving the sphenoid sinus and the clivus, with lateral skull base extension. B: Lymphoplasmocellular infiltration with fibrous scarring and bony erosion on hematoxylin and eosin stain.

thus carried out prior to a type C infratemporal fossa approach.¹⁵ A noncapsulated, infiltrative process was encountered in the infratemporal fossa involving the soft tissues and the trigeminal nerve. There was significant adherence of this process to the bony skull base, with extensions into the clivus and sphenoid sinus. Multiple biopsies were taken for frozen section analysis, and no malignant tissues were identified. Resection appeared complete using the standard type C approach. The horizontal segment of the internal carotid artery was not involved in this process and was therefore left in situ. Surgical cavity was obliterated with temporalis muscle and abdominal fat.

Histologically, a chronic lymphoplasmocellular inflammation and fibrous scarring were seen with bony involvement (Fig. 2B). This histologic picture has been called plasma cell granuloma in the past,⁷⁻¹⁰ in spite of the lack of epithelioid granulomas. A striking siderosis in the tissue was noted, but there was no evidence of malignancy by other histologic criteria or by immunohistochemistry. The patient is well and without recurrence for 2 years. He has some residual trigeminal paresthesia.

Case 3 (GJ)

A 44-year-old man presented in April 1990 with a 1-year history of fullness and tinnitus of the left ear. Examination revealed a left sided middle ear effusion with a conductive hearing loss of 30 dB on audiogram; the contralateral ear was unremarkable. He also demonstrated paresthesia in the mandibular distribution of the trigeminal nerve. On direct nasopharyngoscopy, swelling in the region of the left tubal orifice was noted without any mucosal disease. The patient had no lymphadenopathy or other abnormalities on examination. A CT (Fig. 3A) and MRI confirmed a 2-cm peritubal lesion that was not clearly demarcated. The pterygoid muscles and the foramen ovale region appeared involved. A biopsy of the nasopharyngeal swelling demonstrated only chronic inflammatory changes. In view of this clinical and radiographic presentation, a nasopharyngeal malignancy was suspected in spite of a negative biopsy. A type C infratemporal fossa approach was carried out. This approach was chosen to provide better exposure of the lateral skull base, especially in the region of the foramen ovale and the petrous carotid artery. Its use in tumors of similar locale has been documented previously.¹⁵

A peritubal inflammatory-fibrous process was encountered, with infiltration of the mandibular nerve. The involved soft tissues of the infratemporal fossa and pharyngeal tubal orifice were resected en bloc. Surgical defect was then reconstructed with the temporalis muscle in the standard fashion.

The excised tissues showed abundant chronic inflammation with a fibrous and sclerosing connective tissue component. Scattered granulomalike nodules exhibited

central necrosis with accumulation of granulocytes. With these microabscesses no bacterial, fungal, or parasitic remnants could be identified with special staining (Gram, Ziehl-Neelsen, Grocott). There were no blood vessels seen neighbouring the granulomas, nor were there vasculitic changes to suggest Wegener's granulomatosis. The final diagnosis was sclerosing inflammatory pseudotumor (Fig. 3B). The patient is now 20 months post-op without recurrence. He has an expected trigeminal (mandibular) paresthesia, with a conductive hearing loss on the operated side.

DISCUSSION

The challenges of skull base surgery have been in most part related to technical considerations—specifically, in limiting surgical morbidity. Occasionally, diagnostic dilemma becomes an issue, as seen in the three cases of inflammatory pseudotumors reported in this study. This difficulty is primarily attributable to the relatively inaccessibility of lesions to conventional biopsy techniques. Furthermore, clinicians are often unwilling to accept the diagnosis of inflammation in the presence of a clinically aggressive disease. Given the rarity of pseudotumors, it is axiomatic that such specimens be carefully scrutinized to avoid misdiagnosis.

When inflammation is the predominant feature in a biopsy specimen, a neoplastic process must be ruled out. First, an epithelial tumor with severe inflammation should be considered. Multiple biopsies will reduce sampling error; the use of pancytokeratin antibodies and epithelial membrane antigens (EMAs) may detect small strands of tumor cells. In younger patients, a sarcoma must be suspected by carefully analyzing the proliferating characteristics of the mesenchymal component, especially in tumors with a predominantly inflammatory and fibrous background.

Immunohistochemistry and electron microscopy are expendable tools in confirming tumors such as rhabdomyosarcomas. If a monotonous lymphoplasmocytic picture is identified without a conclusive morphology, a lymphoproliferative disorder must be excluded. If histiocytosis is suspected, Langerhans histiocytes can usually be identified by S100 immunostain. Likewise, granulomatous inflammation such as Wegener's granulomatosis, midline lethal granuloma, and atypical infections need to be considered. From a practical point of view, the diagnosis of inflammatory pseudotumor of the skull base could only be made after having systematically excluded other possibilities.

There have been several histologic classifications of pseudotumors based on cellular composition.^{16,17} Henderson's original classification¹⁸ has been the most widely accepted, describing two histologic patterns commonly seen in orbital pseudotumors. Type 1, a less common variety, is marked by vasculitis and cellular response of

Figure 3. A: Coronal computed tomography scan with contrast. An enhanced region (T) involving the lateral skull base at the level of the foramen ovale. B: Sclerosing inflammation with a predominantly lymphoplasmocytic component. No evidence of infectious remnants identified on this Ziehl-Neelsen stain.

diffuse polymorphonuclear leukocyte infiltration with predominantly eosinophils in the acute phase. Type 2 is more common and displays a predominantly lymphocytic cellular response, with fibrosis in the chronic stage.

Henderson has recently decided that the type 1 group is a variant of vasculitis, and has further subdivided type 2 histology into three subgroups⁶; these include (1) diffuse lymphocytic, (2) mixed lymphocytic-fibrotic, and (3) predominantly fibrotic pictures. It seems that these three patterns represent a continuum of an inflammatory process beginning with an active phase that develops into a fibrovascular stage, and then eventually burns itself out.

Pseudotumors have no distinctive characteristics either clinically or radiographically. Experience gained in the management of orbital pseudotumors has shown that extensive systemic reviews supplemented by laboratory tests have not been successful in producing a constant

diagnostic picture.⁶ The etiology of pseudotumors remains speculative. The role of chronic infection or immunologic response has not been clearly elucidated.

Pseudotumors behave like other space-occupying lesions, producing symptoms of compression, displacement, pain, and restriction of movement. Radiographically, they may appear infiltrative, solid, diffuse, or circumscribed. Bony erosions and cranial neuropathy are uncommon findings in orbital pseudotumors except in recalcitrant lesions of long duration, and they are usually located in the orbital apex.^{1,2,4,5,6} Pseudotumors of the skull base, on the other hand, are usually indistinguishable from aggressive neoplasms.^{1,2,11,12} Bony erosion, soft tissue infiltration, and neuropathy are frequent findings, and are features suspicious of invasive or malignant neoplasms.

Treatment of inflammatory pseudotumors has mainly developed along three paths—namely, surgery, radio-

therapy, and systemic steroid therapy. In orbital disease, a pretreatment diagnosis is usually available due to surgical accessibility. It is known that patients with mild orbital presentations often undergo resolution spontaneously or following steroid treatment within a matter of months. Severe and progressive diseases, however, appear best treated by surgery with complete excision, provided that accessibility and adequate cleavage planes from vital structures can be obtained.⁶ Patients with poor prognosis generally have severe or chronic disease at presentation, and in these cases and in those with incomplete resections, radiotherapy (3.5–6.0 Gy) may be beneficial in halting further growth and inflammatory destruction.^{6,19} Steroids have been shown to produce a salutary effect but may only temporarily suppress the inflammatory process. Responses to steroid therapy in extraorbital pseudotumors are unpredictable and generally ineffective in those containing significant fibrosis or those of a long-standing duration. Another word of caution with steroid treatment is that malignancies with a large inflammatory component as well as lymphoproliferative diseases may undergo a reduction in size, giving a false impression of treatment benefit. A 6-week course of steroid treatment commonly recommended for pseudotumors in the presence of a seemingly malignant process can have serious consequences.

The accurate diagnosis of inflammatory pseudotumor remains the biggest challenge in its management. At this point, the most important issue is to obtain adequate specimens for diagnosis, while retaining the option to carry out a complete resection that is oncologically sound. Techniques such as subtotal petrosectomy and infratemporal fossa approaches are well established and have played an important role in the management of benign and malignant diseases of the skull base.¹⁹

It must be emphasized that the diagnosis of inflammatory pseudotumor of the skull base can be extremely difficult to establish preoperatively. In view of its rarity, inflammatory pseudotumor must remain a diagnosis of exclusion.

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